SUPPLEMENTARY INFORMATION

Kaiser Permanente Northern California (KPNC) Study Subjects: MS cases were identified through electronic health records (EHR), as any KPNC member with at least one outpatient diagnosis of MS by a neurologist (multiple sclerosis, ICD9 code 340.xx); 95% had at least two MS diagnoses by a neurologist at study entry. MS cases met well-established disease criteria, as defined by McDonald et al. [1], confirmed by neurologist, through review of EHR data and patient interviews. All participants were 18-69 years of age and KPNC members at the time of initial contact. The average MS case participation rate for the KPNC MS Research Program is ~80%. Cases for this study were drawn from current KPNC MS Research Program participants. They were selected on the basis of age and their TICS-M scores, a general cognitive screening test [2], collected at study entry. A representative sample of MS cases with a range of cognitive function based on TICS-M scores and age were studied. Potential participants received a letter with a follow-up phone call, explaining the study goals and procedures. Those who agreed to participate were e-mailed a secure link and password for on-line data collection prior to cognitive function testing. Questions for on-line collection included the MS Neuropsychological Screening Questionnaire [3], and additional questions about general health and life-style habits.

University of Buffalo (UB) Study Subjects: We applied an automated routine within the Statistical Analysis System (SAS 9.4) to create randomly matched control and MS case pairs to the KPNC MS participants. An archival database including baseline

evaluations from active studies on the effects of pharmacotherapy on cognition in MS, was utilized to acquire matches for the current study. The UB database comprised 318 controls and 1,425 MS patients with in-person CVLT-II assessments who have been previously described [4-10].

Remote cognitive assessment protocol. Each KPNC MS patient received a letter of invitation to participate. The letter explained that many people with MS experience cognitive symptoms and the purpose of the study was to learn more about what causes these important symptoms. At the time of scheduling, each participant was asked to set aside time and a private location for remote cognitive testing. They were not told ahead of time any details about the test. Our most experienced staff interviewer was formally trained in administering the CVLT-II and conducted all of the remote CVLT-II assessments using the same procedure. At the beginning of each assessment the interviewer obtained informed consent, confirmed study participants were not driving a car and were alone. The interviewer determined whether there was background noise (TV, other) and required the participants to eliminate this source of distraction if it was detected. Brief instructions were then given as follows: *"I am going to read a list of 16 words to you. After I finish reading the list, I want you to repeat back to me as many of the words you can remember in any order. If there is a word you didn't understand, just repeat it back to me as close as possible. We will repeat this exercise 4 more times for a total of 5 times"*. Participants were told there were no consequences of doing well or poorly. Participants were told they should not write down the words. The interviewer recorded all answers using our web interface to minimize error, and also recorded notes on each assessment at the end of the session. Each time the patient repeated words back to the interviewer, the order was noted by the interviewer to help determine the words were being recalled from memory rather than being recorded by the participant. Three of 90 MS patients asked whether they could record the words before the

assessment started; they were reminded of the instructions. Regular meetings with the research team were scheduled to debrief each interview. The interviewer did not observe any evidence that suggested patients were recording the words during the assessment. The interviewer's experience also included previously administering the Modified Telephone Interview for Cognitive Status (TICS-M), a previously validated phone assessment to detect mild cognitive impairment in health elderly individuals, to more than 2,000 KPNC MS patients and controls as part of an earlier study[11].

Study protocols were approved by the Institutional Review Boards at UC Berkeley, Kaiser Permanente Division of Research and UB. All study participants provided informed consent.

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